study. Further study is warranted for a causal link between general sickness and specific cytokines during human GVHD development.

Table 1. *Correlations between Symptom Severity and IL-8 Levels before and after the Development of GVHD in the First 100 Days after Allo-BMT*

Symptom	Correlation with IL-8 Levels
Pre-GVHD	
Shortness of breath	$r = -0.708$, $P < .01$
Dry mouth	$r = 0.667$, $P < .05$
Sadness	$r = 0.631$, $P < .05$
Post-GVHD	
Sleep disturbance	$r = 0.564$, $P < .05$
Drowsiness	$r = -0.565$, $P < .05$
Vomiting	$r = -0.558$, $P < .05$

10

INCREASED CLEARANCE OF *ASPERGILLUS FUMIGATUS* IN MICE WITH CHRONIC LUNG INJURY AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

Hildebrandt, G.C.[1], Olkiewicz, K.[2], Hogaboam, C.M.[3], Ferrara, J.L.[2], Cooke, K.R.[2] [1]Department of Hematology and Oncology, University of Regensburg Medical School, Regensburg, Germany; [2]Department of Pediatrics, University of Michigan Medical School, Ann Arbor, MI; [3]Department of Pathology, University of Michigan Medical School, Ann Arbor, MI.

Chronic lung injury (CLI) is a frequent problem after allogeneic (allo) stem cell transplantation (SCT) leading to obstructive and/or restrictive changes in lung function. CLI is associated with significant morbidity and mortality and is frequently complicated by co-existing opportunistic infections. We developed a murine SCT model of CLI by transplanting splenocytes and bone marrow cells from G-CSF treated syngeneic (syn) B6D2F1 or allo C57BL/6 donor mice into lethally irradiated B6D2F1 recipients. Animals were analyzed between day 90 and 100 after transplant. Allo but not syn recipients showed typical changes of CLI: pulmonary resistance was significantly increased (146 ± 12 vs. 106 ± 5%), and lung compliance was decreased (62 ± 6 vs. 77 ± 3%) compared to syn controls ($P < .01$) Functional changes correlated with significant histopathology, including a dense mononuclear cell infiltrate around bronchial structures (score: 5.3 ± 0.7 vs. 0.3 ± 0.3; $P < .01$), peribronchial fibrosis and pulmonary collagen deposition. Histopathologic changes were associated with increased numbers of BALF total cells (1.68 ± 0.26 vs. 0.89 ± 0.08 × 10^6; $P < .01$), and both CD4+ (2.9 ± 0.4 vs. 1.4 ± 0.1 × 10^5; $P < .01$) and CD8+ T cells (1.0 ± 0.1 vs. 0.1 ± 0.0 × 10^5; $P < .01$). Interestingly, IFN-γ+ CD4+ and IFN-γ CD8+ T cells and lung mRNA for CCR2 were also increased indicating a local proinflammatory environment. Next we determined whether animals with CLI after allo-SCT were more susceptible to fungal infection than syn controls. SCT recipients were injected intratracheally with 5 × 10^6 *Aspergillus fumigatus* (A.f.) conidia around day 70 and were analyzed 3 weeks later. Surprisingly, recipients of allo-SCT showed increased pulmonary clearance of A.f. with significant reductions of conidia within the bronchial epithelium and of associated goblet cell hyperplasia compared to syn controls. **Conclusion:** Despite the development of significant CLI, allo-SCT recipients have enhanced clearance of A.f. conidia compared to syn controls. These data suggest that the proinflammatory micro-environment associated with non-infectious lung injury after SCT may have a heretofore unidentified beneficial effect on immune surveillance, perhaps calling into question the merits of continuing systemic immunosuppression in patients with CLI without evidence for clear improvements in lung function.

11

DONOR-SPECIFIC CELL ENGRAFTMENT AFTER INTRAOSSEOUS AND INTRAVENOUS BONE MARROW TRANSPLANTATION

Klimczak, A.[1], Unal, S.[1], Jankowska, A.[1], Coburn, C.[1], Siemionow, M.[1] [1]The Cleveland Clinic Foundation, Cleveland, OH.

Background: Engraftment of donor-derived bone marrow cells into recipient bone marrow environment can induce hematopoietic chimerism and tolerance to antigen-matched organs in solid organ and composite tissue allograft. This study was designed to investigate the effect of intraosseous bone marrow transplantation (BMT) for donor cells engraftment into the bone marrow environment and lymphoid tissue compartment across MHC barrier under short-term αβ-TCRmAb/CsA protocols. **Materials and Methods:** Forty-eight BMT were performed between ACI ($RT1^a$) donors and LEW ($RT1^l$) recipients. Intraosseous and intravenous BMT was studied in 6 groups of 8 animals each receiving 35 × 10^6 (n = 4) and 70 × 10^6 (n = 4) bone marrow cells. Groups I and II (controls) received BMT but no treatment, groups III and IV CsA monotherapy, and groups V, VI αβ-TCRmAb/CsA protocol for 7 days. Flow cytometry monitored immunodepletion and donor-specific chimerism for MHC class I ($RT1^a$) antigens in the peripheral blood and bone marrow compartment. Immunocytochemical staining was employed to detect the presence of donor-derived cells in the lymphoid tissue of recipients. **Results:** All animals survived without the occurrence of graft versus host disease. Short term αβ-TCRmAb/CsA protocol and 70 × 10^6 bone marrow cells delivery resulted in 7.9% ± 1.3% of donor cell engraftment after intraosseous BMT compared to 4.2% ± 1.4% after intravenous transplantation. Donor bone marrow cell engraftment into the recipient bone marrow compartment delivered via the intraosseous route under the αβ-TCRmAb/CsA protocol was 40% more efficient after 70 × 10^6 bone marrow cell transplantation compared to 35 × 10^6 (7.9% vs 4.8% respectively). Also, CsA monotherapy and 70 × 10^6 bone marrow cell delivery resulted in better engraftment of donor cells after intraosseous transplantation compared to 35 × 10^6 of BMT (3.8% vs 2.2% respectively). Donor-derived cells were present in the lymph nodes and spleen of recipients. Higher seeding efficiency of donor cells into the lymphoid tissue compartment was achieved after intraosseous BMT and αβ-TCRmAb/CsA protocol compared to standard intravenous transplantation. **Conclusion:** Intraosseous transplantation of donor bone marrow cells under αβ-TCRmAb/CsA protocol was more effective for donor cell engraftment into recipients' bone marrow environment and lymphoid tissue compartment compared to intravenous transplantation.

12

ALLOGENEIC TRANSPLANTATION FOR ADULT ACUTE LYMPHOBLASTIC LEUKEMIA: INTENTION TO TREAT ANALYSIS OF THE EORTC ALL-4 PHASE III TRIAL

Labar, B.[1], Suciu, S.[2], Muus, P.[3], Willemze, R.[4], Marie, J.-P.[5], Fillet, G.[6], Berneman, Z.[7], Jaksic, B.[8], Feremans, W.[9], Bron, D.[10], Sinnige, H.[11], Mistrik, M.[12], Vreugdenhil, G.[13], De Bock, R.[14], Nemet, D.[1], Gilotay, C.[2], De Witte, T.[3], Amadori, S.[15] [1]University Hospital Center Rebro, Zagreb, Croatia; [2]EORTC Data Center, Brussels, Belgium; [3]St. Radboud University Hospital, Nijmegen, The Netherlands; [4]Leiden University Hospital, Leiden, The Netherlands; [5]Hotel-Dieu de Paris, Paris, France; [6]CHU Sart-Tilman, Liege, Belgium; [7]Universitair Ziekenhuis Antwerpen, Antwerpen, Belgium; [8]Clinical Hospital Merkur, Zagreb, Croatia; [9]Hopital Universitaire Erasme, Brussels, Belgium; [10]Institut Jules Bordet, Brussels, Belgium; [11]Groot Ziekengasthuis, Den Bosch, Netherlands; [12]University Hospital, Bratislava, Slovakia (Slovak Republic); [13]St. Josef Ziekenhuis, Veldhoven, The Netherlands; [14]Algemeen Ziekenhuis Middelheim, Antwerpen, Belgium; [15]Ospedale San Eugenio, Rome, Italy.

Results of the EORTC ALL-3 reveal that the policy to perform allo-SCT in a case when a sibling donor is available does not result in a significantly better outcome than to offer auto-SCT or continuous maintenance. We also analysed the outcome of allografted patients in EORTC ALL-4. In this trial patients were randomized to receive either dexamethasone (10 mg/m^2/day) or 6-methylprednisolone (60 mg/m^2/day) on days 1-8 and 15-22 with standard